REMARKS

First, Applicants wish to thank the Examiner for a thorough and thoughtful examination of the claims.

Claims 16-21 are pending. Claims 1-15 and 22-38 are withdrawn from consideration as being drawn to non-elected subject matter. New Claims 39-68 have been added herein and Claims 16-18 have been amended. Upon entry of these amendments, Claims 16-21 and 39-68 will be pending and under consideration in the instant application.

Applicants acknowledge that process claims of Groups II and III can be rejoined pursuant to M.P.E.P. § 821.04 once product claims of Group I are allowed. As suggested by the Examiner in the Office Communication (Restriction Requirement) mailed March 11, 2004, Applicants have amended currently withdrawn Claims 1, 8 and 23-27 consistent with the amendments of Claims 16-17. Applicants reserve the right to rejoin Claims 1-15 and 22-38 currently withdrawn from consideration.

I. AMENDMENTS TO THE CLAIMS

Claims 1, 8, 16-17 and 23-27 have been amended to include the phrase "a purified" with regard to ApoA-I protein. Support for these amendments can be found, for example, on page 12, line 5 through page 14, line 11 of the specification. Additionally, Claim 16 has been amended to spell out Apolipoprotein A-I (ApoA-I) protein, as suggested by the Examiner. Claim 17 has been amended to recite in relevant part "[w]herein said complex activates LCAT (lecithin cholesterol acyl transferase) activity, promotes cholesterol efflux and is suitable for administration in humans." Support for this amendment can be found on page 8, lines 16-25 of the specification.

New Claims 39-42 are drawn to a pharmaceutical composition of Claim 16 wherein a non-human animal ApoA-I protein has greater than about 38%, 40%, 43% or 45% human LCAT activation activity, respectively. Support for newly added Claims 39-42 can be found on page 9, lines 18-21. New Claims 43-45 are drawn to a pharmaceutical composition of Claim 16 having at about 1 to about 350 mg of ApoA-I protein. Support for new Claims 43-45 can be found on page 20, lines 9-17. New Claims 46-49 are drawn to a pharmaceutical composition of Claim 16 wherein a non-human ApoA-I protein is derived from bovine, chicken, turkey and porcine. Support for new Claims 46-49 can be found on page 4, lines 21-26. New Claims 50-53 are drawn to a pharmaceutical composition of Claim 16 wherein a non-human animal ApoA-I protein having greater than about 60%, 70%, 80% or 90%

homology with native human ApoA-I protein, respectively. Support for new Claims 50-53 can be found on page 9, lines 22-29. New Claims 54-56 are drawn to an ApoA-I protein-lipid complex of Claim 17 having at about 1 to about 350 mg of ApoA-I protein. Support for new Claims 54-56 can be found on page 20, lines 9-17. New Claims 57-60 are drawn to an ApoA-I protein-lipid complex of Claim 17 wherein a non-human animal ApoA-I protein has greater than about 38%, 40%, 43% or 45% human LCAT activation activity, respectively. Support for new Claims 57-60 can be found on page 9, lines 18-21. New Claims 61-64 are drawn to an ApoA-I protein-lipid complex of Claim 17 wherein non-human animal ApoA-I protein having greater than about 60%, 70%, 80% and 90% homology with native human ApoA-I protein, respectively. Support for newly added Claims 61-64 can be found on page 9, lines 22-29. New Claims 65-68 are drawn to an ApoA-I protein-lipid complex of Claim 17 wherein a non-human ApoA-I protein is derived from bovine, chicken, turkey and porcine. Support for new Claims 65-68 can be found on page 4, lines 21-26. Therefore, no new matter has been introduced by these amendments. Accordingly, entry of the above-mentioned amendments is kindly requested.

II. THE REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 16-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner suggests that in Claims 16-21 Apolipoprotein A-I (ApoA-I) needs to be spelled out in the first instance of use.

Applicants have amended Claim 16 to recite "A pharmaceutical composition comprising ....non-human animal Apolipoprotein A-I protein (ApoA-I protein)...", as suggested by the Examiner. Accordingly, it is respectfully requested that the rejection be withdrawn.

III. THE REJECTION UNDER 35 U.S.C. §101

Claims 16-21 are rejected under U.S.C. 101 because the claimed invention allegedly directed to non-statutory subject matter. In particular, the Examiner is of the opinion that the polypeptide as claimed, has an amino acid sequence duplicative of that of the non-human animal ApoA-I protein or the cellular precursor thereof and possesses the biological and functional properties of the naturally occurring polypeptide ApoA-I, and, therefore, does not constitute patentable subject matter absent recitation of "isolated and purified" in the

preamble. This rejection is traversed and the following discussion is offered in response.

First, Applicants respectfully submit that they are not claiming protein *per se*. Instead, Claims 16 and 18-21 are drawn to a pharmaceutical composition. The pharmaceutical composition of Claims 16 and 18-21 cannot read on a "naturally occurring" protein since the claim requires that the active ingredient be in a composition and in a form suitable for administration to humans. To the extent that this rejection questions patentability of a purified protein in a pharmaceutical composition, Applicants refer the Examiner, for example, to the decision *In re Kratz*, 592 F.2d 1169 (1979), wherein The Court of Customs and Patent Appeals discusses in detail that the language of a claim is an important consideration in determining whether a claim reads on a products of nature. *Kratz*, at 1173-1174. Here, as in *Kratz*, a composition of a pure material is claimed and thus the claim is patentable under 35 U.S.C. §101. In other words, the non-human animal protein of the instant invention used in a pure form as an active ingredient in the pharmaceutical composition differs from the naturally occurring non-human animal polypeptide ApoA-I. As such, it qualifies as a "non-naturally occurring manufacturer or composition of matter having a distinctive name, character, [and] use", and is patentable subject matter. MPEP 2105.

The same arguments apply with regard to Claim 17. Nevertheless, in order to expedite prosecution, Claims 16 and 17 have been amended to recite in a relevant part "...a purified non-human animal ApoA-I protein...", as suggested by the Examiner. Accordingly, it is respectfully requested that the rejection be withdrawn.

IV. THE REJECTION UNDER 35 U.S.C. §102(b)

Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by Shackelford and Lebherz (Shackelford, J. and Lebherz, H. "Synthesis and Secretion of Apolipoprotein A_1 by Chick Breast Muscle", *The Journal of Biological Chemistry* 258(11):7175-7180 (1983)). In particular, the Examiner states that Shackelford and Lebherz disclose a non-human animal ApoA-I protein and a lipid therefore teaching all the elements of Claim 17, and thus Claim 17 is anticipated under 35 U.S.C. 102(b). This rejection is respectfully traversed. Reconsideration is kindly requested.

Claim 17 now recites "A non-human animal ApoA-I protein-lipid complex comprising a purified non-human animal ApoA-I protein and a lipid wherein said complex activates LCAT (lecithin cholesterol acyl transferase) activity, promotes cholesterol efflux and is suitable for administration in humans." As amended, Claim 17 particularly points out

and distinctly claims the invention, *e.g.,* the ApoA-I protein/lipid complex based on a purified non-human animal ApoA-I protein, which complex is capable of LCAT activation activity and cholesterol efflux. These features are highly relevant for medications used for treatment of dyslipidemic disorders including cardiovascular disease, coronary artery disease, atherosclerosis and restenosis. The fact that the claimed protein/lipid complex promotes cholesterol efflux means that the complex has the ability to act as a scavenger of tissue cholesterol and provoke cholesterol clearance from the body. Finally, the claimed ApoA-I protein-lipid complex contains purified non-human animal ApoA-I protein.

To sustain an anticipation rejection, Shackelford and Lebherz must disclose each element of the claimed invention. However, the cited reference does not disclose a peptide:lipid complex as claimed, much less a purified complex having the required biological activity. Indeed, the cited reference merely reports on the identification of an "ApoA-I:like protein from chicken muscle", and proposes an explanation for the presence of the endogenous material. As such, the ApoA-I protein complex of Claim 17 clearly distinguishes from the endogenous Apo-A_1-like protein cited by the Examiner. Therefore, Shackelford and Lebherz do not disclose each and every element of the claimed invention. Thus, Shackelford and Lebherz cannot anticipate Claim 17 as amended under 35 U.S.C.§ 102 (b). Accordingly, it is respectfully requested that the rejection be withdrawn.

V. THE REJECTION UNDER 35 U.S.C. §103

Claims 16 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shackelford and Lebherz in view of Dasseux *et al.* (U.S. Patent 6,037,323). The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a complex of non-human protein and lipid, as disclosed by Shackelford and Lebherz, and use this complex in a manner of a pharmaceutical composition in a form of a lyophilized powder because of the benefits taught by Dasseux *et al.* of administration of lyophilized powders. This rejection is respectfully traversed. Reconsideration is kindly requested.

First, Applicants would like to thank the Examiner for clarification provided during the telephone communication on August 11, 2004.[1] As confirmed during the call, Claim 17 was rejected by the Examiner only under 35 U.S.C. 102(b) and not under 35 U.S.C. 103(a).

[1] Claim 18 is now dependent from Claim 17.

The Examiner agreed to consider arguments presented for non-obviousness of Claim 17.

In determining whether a case of *prima facie* obviousness exists, it is necessary to ascertain whether the prior art teaching would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed modification. The prior art must provide one of ordinary skill in the art the motivation to make the proposed modifications needed to arrive at the claimed invention. *See In re Lalu*, 747 F.2d 703, 223 USPQ 1257 (Fed. Cir. 1984). In reversing the obviousness rejection the court held:

> "An element in determining obviousness of a new chemical compound is the motivation of one having ordinary skill in the art to make it. The motivation is not abstract, but practical, and is always related to the *properties or uses* one skilled in the art would expect the compound to have, if made. ... The present obviousness rejection cannot stand without some basis in the expected properties of the claimed compounds."

The Shackelford and Lebherz's reference discloses an Apo-A_1-like protein derived from a chicken breast muscle which is capable of association with a lipid. Claims 16-20 are drawn to a non-human animal ApoA-I protein-lipid complex having LCAT activity, which promotes cholesterol efflux and is suitable for administration in humans, and a pharmaceutical composition comprising such complex. The cited reference provides no teaching or suggestion that the ApoA-I-like molecule from chicken could be used as a therapeutic for the treatment of cholesterol related disease in a human. Indeed, at the time of the reference, there was no teaching or suggestion that such a protein had any therapeutic benefit, much less any suggestion to associate it with a lipid and then use it as a therapeutic. *See In re Rouffet*, 149 F.3d 1350,1357, 47 USPQ2d 1453, 1457-1458 (Fed. Cir. 1998). At best, the art cited by the Examiner gives rise to an "obvious to try" the protein in a screen for activity. However, as the Examiner is well aware, this is not the proper standard. *See In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

Further, Shackelford and Lebherz discuss neither LCAT activation activity of their protein, much less the use of a peptide/lipid complex to achieve cholesterol efflux and its clearance from the body. The reference provides no suggestion of the use of the peptide/lipid complex as a pharmaceutical ingredient useful to treat dyslipidemic disorders in different species, including humans. This lack of teaching of therapeutic activity in the cited reference confirms that there is no suggestion or motivation to make the modifications needed to arrive

at the claimed invention, and thus does not render the instant invention obvious. *In re Lalu*, 747 F.2d at 1257.

Dasseux *et al.* does not remedy the deficiencies of Shackelford and Lebherz. Indeed, Dasseux teaches away from natural material by emphasizing the benefits of specific synthetic peptides over natural proteins. The Dasseux' sequences of small non-natural peptides are not related to the natural non-human compounds of the instant invention.[2] Neither of citation alone or in combination teaches or suggests a purified non-human animal ApoA-I protein/lipid complex and a pharmaceutical composition comprising such complex as claimed in the instant invention, and thus does not render the instant invention obvious. Accordingly, it is respectfully requested that the rejection be withdrawn.

CONCLUSION

Applicants submit that Claims 16-21 and 39-68 satisfy all the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly solicited.

No fee is believed to be due at this time. However, if the Office determines that a fee is, in fact, due, pursuant to 37 C.F.R. §1.136 (a)(3), the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. §1.17 and all required extension of time fees, or credit any overpayment, to Jones Day U.S. Deposit Account No. 503013 (Attorney Docket No. 10173-084-999).

Respectfully submitted,

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[2] Since Dasseux *et al.* provides no discussion of non-human natural peptides, there is no motivation to use non-human natural peptides at all, and one may argue that there is no motivation to combine the references cited by the Examiner. *See In re Fritch*, 972 F.2d 1260, 23 USPQ2d 1780 (Fed. Cir. 1992).